

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 2005/001336

## A. CLASSIFICATION OF SUBJECT MATTER

IPC: see extra sheet  
 According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE, DK, FI, NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-INTERNAL, WPI DATA, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 20020061879 A1 (DAVID S. GARVEY ET AL), 23 May 2002 (23.05.2002), paragraphs (0002); (Q008)-(0010); (0012); (0123); (0125)-(0130); (0137)-(0141); (0150)-(0151); (0153); claims 9-10, 12-16, 24-30  --	1-3, 10, 13-14, 16, 18, 22-32, 34-40
X	US 20040162243 A1 (PRZEMYSŁAW A. MAREK ET AL), 19 August 2004 (19.08.2004), paragraphs (0002); (0008); (0043)-(0045); (0133)-(0137); (0146)-(0150); (0160); (0162); (0164); (0167)-(0169); (0174); claims 5-6, 8-10, 14-16  --	1-3, 10, 22-40

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

26 January 2006

Date of mailing of the international search report

30-01-2008

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**C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 0057891 A1 (TRUSTEES OF BOSTON UNIVERSITY), 5 October 2000 (05.10.2000), page 1, line 8 - line 21; page 16, line 23 - page 18, line 3; page 19, line 11 - page 20, line 21, page 24, lines 4-14; page 25, line 11-page 26, line 29; claims 2-3,7-9,29-30,34-35,46-47,51-52, 65-67  --	1-3,10,22-40
X	US 20030050305 A1 (INIGO SAENZ DE TEJADA), 13 March 2003 (13.03.2003), paragraphs (0002); (0038)-(0041); (0132)-(0136); (0144)-(0147); (0161); (0163); (0165); (0167)-(0175), claims 16-17,19-21,49-50,53-54  --	1-3,10,22-40
X	US 6417162 B1 (DAVID S. GARVEY ET AL), 9 July 2002 (09.07.2002), paragraphs (0003); (0008); (0128); -(0131);(0139)-(0143);(0152)-(0155) claims 10-11, 13-17  --	1-3,10, 13-14,16,18, 22-32,34-40
X	WO 9638136 A1 (NITROMED, INC.), 5 December 1996 (05.12.1996), page 9, line 13 - page 11, line 24; page 22, line 10 - page 24, line ZZ \ page 29, line 1 - page 31, line 7, page 36, lines 8-20; page 38, line 10-page 40, line 7 ; claims 1-50  --	1-3,10,22-40
X	US 6352709 B1 (JONATHAN S. STAMLER ET AL), 5 March 2002 (05.03.2002), column 5, line 10 - line 20; column 5, line 34 - column 6, line 2; column 10, line 58 - column 11, line 55, column 15, line 24 - column 17, line 8 ; column 18, lines 53-65; column 19, line 30 - column 20, line 24; column 21, lines 42-65  --	1-3,10,22-40
X	WO 9635416 A1 (NITROMED, INC.), 14 November 1996 (14.11.1996), page 9, line 33 - page 11, line 9, page ZZ, line 24 - page 24, line ZZ; page 29, line 1 - page 32, line 23, page 36, lines 8-21; page 39, line 27 - page 40, line 7 ; claims 1-50  --	1-3,10,22-40

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**C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1023900 A2 (BRIGHAM AND WOMEN'S HOSPITAL), 2 August 2000 (02.08.2000) , paragraphs (0003)-(0005) , (0017)-(0018) , (0026) ; (0Q33)-(0034) , (0039) , (0054) , (0081) , (0091), (0109) , (0118) , (0150) , (0153) ,(0182) , claims 1-5  --	1-2,22-25, 27-40
X	wo 9422482 A1 (BIORELEASE TECHNOLOGIES, INC.) , 13 October 1994 (13.10.1994) , page 2, paragraph 4 - page 3, paragraph 3;page 7,paragraph 2;page 9, paragraph 3;page 10, paragraphs 2-3; page 12, paragraph 4 ; page 16, paragraph 3-page 17, paragraph 3 , claims 1-66  --	1-2,22, 27-30,35-40
A	wo 2004026345 A1 (NEW YORK UNIVERSITY) , 1 April 2004 (01.04.2004) , See paragraphs (0020)-(0025) ,,(0031) ,,(0033) ,,(0036) ,,(0042)-(0043) , (0046) ,,(0053)-(0059) ,,(0070)-(0079) ,,(0105)-(0108) , (0115) ,,(0118)(0129)-(0141) , claims 1-27  --	1-2,22-40
A	wo 9967296 A1 (DUKE UNIVERSITY MEDICAL CENTER) , 29 December 1999 (29.12.1999)  --	1-40
A	US 6673338 B1 (ERNST V. ARNOLD ET AL), 6 January 2004 (06.01.2004)  --	1-40
A	US 20020094985 A (ROBERT A. HERRMANN ET AL) , 18 July 2002 (18.07.2002)  -----	1-40

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PCT/SE2 005/00133 6

**INTERNATIONAL PATENT CLASSIFICATION (IPC) :****A61K 33/00** (2006.01)**A61K 47/10** (2006.01)**A61K 47/26** (2006.01)**A61K 47/36** (2006.01)**A61K 47/42** (2006.01)**A61P 11/00** (2006.01)**A61K 9/107** (2006.01)

**INTERNATIONAL SEARCH REPORT**International application No.  
PCT/SE2005/001336**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 29-34 , 39-40  
because they relate to subject matter not required to be searched by this Authority, namely:  

Claims 29-34, 39-40 relate to a method of treatment of the human or animal body by surgery or by therapy, as well as diagnostic methods /Rule 39.1(iv). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compositions.
2.  Claims Nos.: Claims 1-3, 8, 13-14, 16, 18, 20, 22, 26, 35-36 partly claims 10-11, 27-28, 37-38  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent.  
See extra sheet
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

The following separate inventions were identified:

1 : Claims 4-12 and partly claims 1-3, 15, 26-40 directed to compositions comprising sugars .

... / ...

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**International application No.  
PCT/SE2005/001336**Continuation Box IZ. 2**

Present claims 1, 26 and partly claims 27-28 relate to a composition and claims 35-36 and partly 38 to a method defined by reference to a desirable characteristic or property, namely that it comprises a compound capable of forming a reversible bond or association with NO. The claims cover all compositions having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and / or disclosure within the meaning of Article 5 PCT for only a very limited number of such compositions. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lacks clarity (Article 6 PCT) . An attempt is made to define the composition by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to compositions comprising the compounds, or compounds from well defined groups, mentioned in claims 4-25. A search has also been carried out for general terms, such as alcohols, sugars and proteins, and all compounds in table 1 in the description.

In present claims 2-3 and partly claims 27-28 and 37-38 the compound capable of forming a reversible bond or association with NO is specified to a carbohydrate or a compound comprising at least one hydroxyl group. However, the specifications are vague and unclear. The claims relate to an extremely large number of possible compositions. In fact, the claims contain so many options that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. The same is true for claims 8, 13-14, 16, 18, 20, 22 and partly for claims 10-11 (the terms higher carbohydrate polymer and higher polysaccharide) where wide and vague specifications are used.

Consequently, the search has been carried out for those parts of the application which appear to be clear and concise, namely those parts relating to compositions comprising the compounds, or compounds from well-defined groups, mentioned in claims 4-25. A search has also been carried out for general terms, such as sugars, alcohols and proteins, and all compounds in table 1 in the description.

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**Box III**

2 : Claims 13-14, 16-21 and partly claims 1-3, 15, 26-40 directed to compositions comprising alcohols.

3 : Claims 22-25 and partly claims 1-2, 26-40 directed to compositions comprising proteins and amino acids.

A full search has been carried out, which relates to the inventions mentioned above.

The present application has been considered to contain 3 inventions which are not linked such that they form a single general inventive concept, as required by Rule 13 PCT for the following reasons :

The single general concept of the present application is the teaching that the compound capable of forming a reversible bond or association with gaseous nitric oxide (NO) is an organic compound comprising at least one hydroxyl group.

Reference is made to the following documents:

US2002061879A1 (D1), US6417162B1 (D2), US2003050305A1 (D3),  
WO0057891A1 (D4), WO9638136A1 (D5), US6352709B1 (D6),  
US2004162243A1 (D8), WO9635416A1 (D7), EP1023900A2 (D9),  
WO9422482A1 (D10)

Document D1-D10 all show that it is known to associate protein and polypeptides with NO. Many of the documents (D1-D8) also show that it is known to associate sugars and NO. In all the documents it is stated that the active form of nitric oxide can be provided by gaseous NO. Further, in D5-D7 and D9-D10 it is explained that the nitrosation can be achieved by exposure to NO gas under anaerobic conditions. This means that compositions for delivery of gaseous NO comprising an organic compound comprising at least one hydroxyl group are known.

Thus, the single general concept is known/obvious and cannot be considered as a single general inventive concept in the sense of Rule 13.1 PCT.

No other features can be distinguished which can be considered as same or corresponding special technical features in the sense of Rule 13.2 PCT.

Thus, the application lacks unity of invention.

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**Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)**

The invention relates to compositions and methods for use in the delivery of gaseous nitric oxide (NO) to a mammal, preferably a human. The compositions for the delivery of the gaseous NO comprise a compound capable of forming a reversible bond or association to NO. Suitable compounds are among others alcohols, carbohydrates and proteins. The nitric oxide is delivered to a mammal for prophylactic and/or therapeutic purposes .

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Information on patent family members

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<b>US</b>	<b>2002</b> 0061879	A1	23/05/2002	AU	721247	B	29/06/2000
				AU	1756297	A	22/08/1997
				CA	2244879	A	07/08/1997
				EP	1018879	A	19/07/2000
				JP	2000505424	T	09/05/2000
				US	5994294	A	30/11/1999
				US	6294517	B	25/09/2001
				US	6323211	B	27/11/2001
				US	6417162	B	09/07/2002
				US	6433182	B	13/08/2002
				US	6469065	B	22/10/2002
				US	6514934	B	04/02/2003
				US	20020143007	A	03/10/2002
				US	20050065161	A	24/03/2005
				US	20050187222	A	25/08/2005
				WO	9727749	A	07/08/1997
				us	5932538	A	03/08/1999
<hr/>							
<b>US</b>	<b>2004</b> 0162243	A1	19/08/2004	us	6762202	B	13/07/2004
				us	20010046471	A	29/11/2001
				AU	6124401	A	20/11/2001
				CA	2408399	A	15/11/2001
				EP	1284653	A	26/02/2003
				WO	0185013	A	15/11/2001
<hr/>							
<b>WO</b>	<b>0057891</b>	A1	05/10/2000	AU	3877800	A	16/10/2000
				US	6589759	B	08/07/2003
<hr/>							
<b>US</b>	<b>2003</b> 0050305	A1	13/03/2003	AU	6472901	A	03/12/2001
				WO	0189519	A	29/11/2001
<hr/>							
<b>US</b>	<b>6417162</b>	B1	09/07/2002	AU	770414	B	19/02/2004
				AU	5701699	A	21/03/2000
				AU	2004201585	A	00/00/0000
				CA	2339145	A	09/03/2000
				EP	1109542	A	27/06/2001
				JP	2002523449	T	30/07/2002
				US	6294517	B	25/09/2001
				US	6323211	B	27/11/2001
				US	6433182	B	13/08/2002
				US	6469065	B	22/10/2002
				US	6514934	B	04/02/2003
				US	20020143007	A	03/10/2002
				US	20050065161	A	24/03/2005
				US	20050187222	A	25/08/2005
				WO	0012075	A	09/03/2000
				AU	721247	B	29/06/2000
				AU	1756297	A	22/08/1997
				CA	2244879	A	07/08/1997
				EP	1018879	A	19/07/2000
				JP	2000505424	T	09/05/2000
				US	5994294	A	30/11/1999
				US	20020061879	A	23/05/2002
				WO	9727749	A	07/08/1997
				US	5932538	A	03/08/1999

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<b>WO</b>	9638136	A1	05/12/1996	AU	6025096	A	18/12/1996
				US	6087479	A	11/07/2000
				US	6174539	B	16/01/2001
				US	6352709	B	05/03/2002
				US	6471978	B	29/10/2002
				US	20030072783	A	17/04/2003
				US	20040037836	A	26/02/2004
<hr/>							
<b>US</b>	6352709	B1	05/03/2002	US	6174539	B	16/01/2001
				US	6471978	B	29/10/2002
				US	20030072783	A	17/04/2003
				US	20040037836	A	26/02/2004
				AU	6025096	A	18/12/1996
				US	6087479	A	11/07/2000
				WO	9638136	A	05/12/1996
				AU	698748	B	05/11/1998
				AU	7831294	A	03/04/1995
				CA	2170772	A,C	23/03/1995
				DE	69433478	D,T	25/11/2004
				EP	0724436	A,B	07/08/1996
				SE	0724436	T3	
				EP	1393723	A	03/03/2004
				JP	9504274	T	28/04/1997
				US	6255277	B	03/07/2001
				WO	9507691	A	23/03/1995
<hr/>							
<b>WO</b>	9635416	A1	14/11/1996	AU	5729596	A	29/11/1996
				US	6255277	B	03/07/2001

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Information on patent family members

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<b>EP</b>	1023900	A2	02/08/2000	SE	1023900	T3	
				DK	1023900	T	06/06/2005
				DK	1023905	T	30/05/2005
				EP	1023905	A ,B	02/08/2000
				SE	1023905	T3	
				EP	1025853	A	09/08/2000
				AU	709725	B	02/09/1999
				AU	2849497	A	16/10/1997
				AU	3071592	A	15/06/1993
				CA	2125037	A ,C	27/05/1993
				DE	69231666	D, T	10/05/2001
				DE	69233474	D	00/00/0000
				DE	69233491	D	00/00/0000
				DK	676964	T	05/02/2001
				EP	0676964	A ,B	18/10/1995
				SE	0676964	T3	
				US	5593876	A	14/01/1997
				US	5863890	A	26/01/1999
				US	6291424	B	18/09/2001
				US	6562344	B	13/05/2003
				US	6583113	B	24/06/2003
				US	20020052314	A	02/05/2002
				US	20030007967	A	09/01/2003
				US	20030211977	A	13/11/2003
				WO	9309806	A	27/05/1993
<hr/>				<hr/>			
<b>WO</b>	9422482	A1	13/10/1994	AU	6523194	A	24/10/1994
				EP	0804244	A	05/11/1997
<hr/>				<hr/>			
<b>WO</b>	2004026345	A1	01/04/2004	AU	2003270689	A	08/04/2004
				US	20040127425	A	01/07/2004
<hr/>				<hr/>			
<b>WO</b>	9967296	A1	29/12/1999	AU	4692999	A	10/01/2000
				CA	2336138	A	29/12/1999
				EP	1093468	A	25/04/2001
				JP	2002518557	T	25/06/2002
				US	6232434	B	15/05/2001
				US	6403759	B	11/06/2002
				US	6673891	B	06/01/2004
				US	6875840	B	05/04/2005
				US	20Q10Q20083	A	06/09/2001
				US	20030078365	A	24/04/2003
				US	20040132904	A	08/07/2004
				US	20050220756	A	06/10/2005
<hr/>				<hr/>			
<b>US</b>	6673338	B1	06/01/2004	US	20040092484	A	13/05/2004
<hr/>				<hr/>			
<b>US</b>	20020094985	A	18/07/2002	CA	2443895	A	25/07/2002
				EP	1399134	A	24/03/2004
				JP	2005503834	T	10/02/2005
				US	6706274	B	16/03/2004
				US	20040171589	A	02/09/2004
				WO	02056864	A	25/07/2002
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